International society of oncology pharmacy practitioners (ISOPP) position statement: The role of oncology pharmacy practitioners in immunotherapy treatment with immune checkpoint inhibitors for malignant conditions

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Abstract
Oncology pharmacists, pharmacy technicians and assistants are key members of the multidisciplinary health care team (MHT) caring for patients receiving immunotherapy with immune checkpoint inhibitors. The International Society of Oncology Pharmacy Practitioners (ISOPP) developed this position statement to provide guidance on the role of oncology pharmacy practitioners in caring for patients receiving immune checkpoint inhibitors.

Four key recommendations were identified:

1) participation as an integrated, collaborative member of the MHT;
2) provision of education and training for patients, students, residents, fellows and other members of the MHT;
3) involvement in clinical governance to optimise the use of immune checkpoint inhibitors and
4) involvement in research and development in the field of immunotherapy.

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In summary, oncology pharmacy practitioners play essential roles within the MHT in caring for patients receiving immune checkpoint inhibitors.

Keywords
oncology pharmacy, pharmacist, immunotherapy, patient care, education, research, immune checkpoint inhibitors, safety, adverse events

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Best practice recommendations for oncology pharmacy practitioners to support immunotherapy treatment in cancer patients

The International Society of Oncology Pharmacy Practitioners (ISOPP) endorses the following:

Statement 1: Oncology pharmacists should participate as an integrated, collaborative member of the multidisciplinary health care team (MHT) for patients receiving immunotherapy with immune checkpoint inhibitors. Oncology pharmacists evaluate appropriateness of clinical indications and the pharmacotherapy plan, including dosing interval, modifications and schedules, review and recommend strategies for managing any related drug, herbal, disease and food interactions, monitor and implement patient-specific management for adverse drug events, and optimise patient adherence to therapy.

Statement 2: Oncology pharmacists play an important role in leading and providing patient-specific education regarding immunotherapy with immune checkpoint inhibitors. Oncology pharmacists should also be involved in education and training on immunotherapy and immune checkpoint inhibitors for pharmacy students, residents, fellows and other members of the MHT. Oncology pharmacy technicians and assistants may also be involved in education and training of pharmacy technicians and assistants and other members of the MHT. Education and training can include didactic education, inclusion in college and university curriculum, and practical training on rotation.

Statement 3: Oncology pharmacy practitioners should be involved, within scope of practice, in clinical governance to support the efficient, safe, effective and optimal use of immunotherapy with immune checkpoint inhibitors.

Statement 4: Oncology pharmacy practitioners should be involved in and support research and development in the field of immunotherapy.

Introduction

The effective treatment of malignant diseases continues to present a significant challenge to international health care systems with global incidence increasing, meaning that more people are now living with and undergoing treatment for cancer. Current global statistics estimate the number of cancer diagnoses at 19.3 million new cases in 2020 with 9.9 million cancer related deaths.

Immunotherapy offers a distinct pharmacological class of treatment which stands apart from conventional therapy modalities. In comparison to traditional chemotherapy where cytotoxic medications are used in controlled doses to induce the destruction of malignant cells, immunotherapy utilises the anti-tumour effect of the patient’s immune system to exert therapeutic activity. Immunotherapy with immune checkpoint inhibitors offers patients with the potential of a different adverse effect profile with improved outcomes when utilised either as monotherapy or in combination with cytotoxic chemotherapy or targeted therapy in tumours when compared to traditional cytotoxic chemotherapy.

Two major classes of immune checkpoint inhibitors, cytotoxic T-lymphocyte associated protein 4 (CTLA-4), programmed cell death protein 1 (PD-1) and programmed cell death ligand 1 (PD-L1) antibodies, have been developed and marketed thus far. A lymphocyte-activation gene 3 (LAG-3) blocking antibody (relatlimab) is under regulatory review in a number of countries. CTLA-4 checkpoint inhibitors (e.g. ipilimumab) binds to CTLA-4 receptors on activated T-cells, thus blocking the inhibitory signal, allowing the cytotoxic T lymphocytes to destroy the cancer cells. PD-1 and PD-L1 checkpoint inhibitors exert therapeutic activity through binding of PD-1 on activated T cells or PD-L1 on tumour cells during the effector phase in peripheral tissue. This modulation of the interaction between PD-1 expressed on lymphocytes and ligands PD-L1 and PD-L2, increases immune mediated tumour destruction and may stimulate a variety of downstream immune cell types to become active against the malignant cells in the tumour microenvironment.

The development of immune checkpoint inhibitors has significantly impacted treatment of many cancers. Currently available medications include ipilimumab,

**Role of oncology pharmacy practitioners in immunotherapy**

The role of oncology pharmacy practitioners (oncology pharmacists, pharmacy technicians and assistants) in this emerging field is also developing, with different health care systems adopting a number of alternative models depending on the clinical requirements of patients, the skills and experiences of oncology pharmacy practitioners, and availability of resources.\(^ {12}\) The advent of immunotherapy and its increasing role in the treatment of malignant disease has highlighted a need for oncology pharmacists to engage with this new treatment modality to ensure that immunotherapy agents are used safely and effectively to treat patients with malignant conditions. In many countries, oncology pharmacists are well established within the wider multidisciplinary team and play a significant role in making treatment recommendations and optimising pharmaceutical care.\(^ {12}\)

ISOPP recognises the work of oncology pharmacy practitioners as experts in the use of medicines, working in the field of immunotherapy, and acknowledges its duty to represent and support oncology pharmacy practitioners to deliver the highest standards of care to patients across the globe. ISOPP commissioned an Immunotherapy Task Force whose objectives were to develop an ISOPP Position Statement on the oncology pharmacy practitioner’s role in the era of immunotherapy, provide education, provide advice on implementation issues in clinical practice and deliver enhanced professional development resources on immunotherapy. The Immunotherapy Task Force has 18 members representing 11 different countries from around the world. (See Appendix 1). The task force completed a survey of members and non-members to identify the current landscape of practice and, together with a literature review, has identified key roles for oncology pharmacists, pharmacy technicians and assistants in the area of immunotherapy.

The Immunotherapy Task Force has identified 4 distinct areas of practice where oncology pharmacy practitioners can play a crucial role in the safe and optimal care of patients receiving immunotherapy.

**Clinical oversight**

Statement 1: Oncology pharmacists should participate as an integrated, collaborative member of the multidisciplinary health care team (MHT) for patients receiving immunotherapy with immune checkpoint inhibitors. Oncology pharmacists evaluate appropriateness of clinical indications and the pharmacotherapy plan, including dosing interval, modifications and schedules, review and recommend strategies for managing any related drug, herbal, disease and food interactions, monitor and implement patient-specific management for adverse drug events, and optimise patient adherence to therapy.

Oncology pharmacists play a number of roles in providing clinical input to the patient’s care and are already well embedded within the cancer multidisciplinary team across global healthcare systems. The antineoplastic drug use process is complex. Medication errors and drug-related problems can arise from prescription to administration and monitoring. Clinicians must ensure that treatment is appropriate for the patient’s diagnosis, hepatic and renal function, that and underlying non-oncologic diseases does not illicit any significant drug interactions with the patient’s other prescribed medications, and that the treatment has a tolerable adverse event profile relative to the patient’s condition, amongst other considerations. Due to the complexities of this process and the inherent risk of managing high risk treatment regimens including antineoplastic drugs, the chemotherapy medication error rate has been reported as 3–16\(^ {13,14}\) versus the medication error rate of non-chemotherapy medications of 2–5\(^ {13,15}\). To mitigate against the potential for patient harm, clinical verification of antineoplastic drug prescriptions by oncology pharmacists has become part of the standard of care within many health care systems and has demonstrated significant benefit in reducing patient harm events.\(^ {14-16}\) A recent review of the literature evaluating the value of oncology pharmacists indicated that a pharmacist may reduce medication errors by as much as 45% and that when pharmacists are involved in patient care, the risk of drug-related morbidity decreased to 6.5% from 26.4\(^ {17}\) (p < 0.001). Although there is a lack of studies documenting the impact of oncology pharmacists for patients receiving immunotherapy treatment regimens, it is likely that pharmacist involvement would help to prevent medication errors and/or near misses related to treatment with immune checkpoint inhibitors.

The implementation of immunotherapy agents as treatment options against malignant disease, alongside developments in other targeted therapies, and incorporation of these new agents in combination with established chemotherapy medications has improved outcomes, but has also increased the potential for adverse events and drug interactions which made us rethink the way of approaching the management of this situation with the propose of to reduce the potential for patient harm events.\(^ {18,19}\) The complexities of identifying
and responding to drug interactions in this context are significant and represent an area in which oncology pharmacists can exert their role as experts in medications to ensure patient safety and tolerance, particularly in patients who take multiple medications to manage coexisting non-malignant conditions. Indeed, a systematic review conducted by Coutsouvelis et al. in 2020 identified that drug interactions were one of the most common interventions undertaken by oncology pharmacists in clinical practice.

Given the novel mechanism of action of immunotherapy, the side effect profiles of these agents differ from those traditionally associated with chemotherapy. Immune-related adverse events (irAEs) are most commonly associated with immunotherapy agents and can vary greatly in presentation, severity and frequency across individual medications and between different patients but can be fatal in 0.3–1.3% of cases. Early identification of potential irAEs and patient counselling are essential in ensuring patient safety and are areas where oncology pharmacists can provide significant benefit. While undertaking routine clinical verification of immunotherapy prescribed regimens, oncology pharmacists are able to review patients biochemical markers, such as a thyroid panel and liver enzyme levels, and identify results or trends which may be suggestive of irAEs.

Published evidence is supportive of the positive impact that oncology pharmacists can play in identifying and managing irAEs. The results from Le et al. describe pharmacists led management of irAEs where the most common interventions included adjustment to patients’ thyroid hormone replacement medications and the initiation and/or titration of medications to manage signs and symptoms of irAE. (Table 1). This study also demonstrated that pharmacist management of irAEs was associated with a reduction in hours per month that physicians spent managing irAEs, suggesting that pharmacist-led services may free clinicians to provide support to patients. Katma et al. describes outcomes of a pharmacist immunotherapy consultation service with 33% of patients requiring pharmacist intervention for managing irAEs. While these studies may be limited in scale, they demonstrate the potential added value of oncology pharmacists as a part of the MHT, the potential for oncology pharmacists to take a lead in the identification and management of irAEs and the role that the profession has to play in the field of immunotherapy. Combination therapy with immune checkpoint inhibitors, including with other immune checkpoint inhibitors, tyrosine kinase inhibitors, chemotherapy and radiation therapy adds to the complexity of the regimen and the potential for adverse events.

The oncology pharmacist’s role in undertaking reviews of patients with irAEs and involvement in subsequent management decisions represents another opportunity for oncology pharmacists to have clinical oversight to improve patient outcomes, particularly around the management of corticosteroids prescribed to treat irAEs. There is still some academic debate around the role that corticosteroids should play in managing irAEs given the potential for their immunosuppressive effects to impair the effectiveness of immunotherapy mediated immune response to malignancies thereby impairing clinical outcomes. However, a recently conducted meta-analysis concluded there was no discernible effect on patient clinical treatment outcomes between immunotherapy and use of corticosteroids. Despite this debate, current clinical practice commonly incorporates use of corticosteroids as a management option for irAEs with between 30–65% of patients receiving corticosteroids for irAEs of grade 3 or above and thus represents another opportunity for oncology pharmacists to provide support to patients. Indeed, the positive role that oncology pharmacists can play in reducing the risk posed by corticosteroids in patients with cancer, particularly around supporting improved glycaemic control, has been formally recognised within recent guidance from the UK Chemotherapy Board.

Patients can experience irAEs at any point during treatment with immunotherapy agents and have been reported in patients several months following discontinuation of treatment. The most commonly reported irAEs which patients experience include skin rashes, headaches, fever and diarrhea and colitis of varying levels of severity. Given the variability in time of presentation and the non-specific nature of symptoms, it is likely that many patients do not recognise these symptoms as signs of possible irAEs despite patient counseling and education. It is therefore also likely that many of these patients present to community or primary care pharmacy services seeking advice and/or over the counter treatment to manage these symptoms. While published evidence to quantify this issue is limited, there is likely a need to support community and primary care pharmacy practitioners to recognise and respond to patients presenting with symptoms of possible irAEs to ensure that opportunities for early detection are not missed.

Education and training

Statement 2: Oncology pharmacists play an important role in leading and providing patient-specific education regarding immunotherapy with immune checkpoint inhibitors to patients, families and caregivers. Oncology pharmacists should also be involved in education and training on immunotherapy and immune checkpoint inhibitors for pharmacy students, residents, fellows and other members of the MHT. Oncology pharmacy technicians and assistants may also be involved in education and training of pharmacy technicians and assistants and other members of the MHT. Education and training can include didactic education, inclusion in college and university curriculum, and practical training on rotation.
In order to maximise the effectiveness and immunotherapy treatments, improve tolerability to some adverse events and reduce the potential for adverse or patient harm events, it is important that healthcare professionals are able to convey clear and consistent information to patients and caregivers. Oncology pharmacists are well positioned to take an active part in providing education to patients to support these principles. The benefits of pharmacist-led patient educational interventions is well recognised in systemic cancer treatments, with published evidence consistently demonstrating that patients report greater insight into their prescribed treatment and understanding of how to correctly use their prescribed medications. 38–40 Recent studies have demonstrated similar outcomes in patients receiving immunotherapy, which provides more evidence towards the crucial role that pharmacist-led patient education intervention plays in this emerging treatment option. 41

Oncology pharmacists also have a significant role in developing and reviewing educational literature developed to provide further support to patients receiving immunotherapy treatments. Wallet cards have been developed to provide patients with easy to access, written instructions reinforcing the information delivered during verbal education sessions. 32,43 There is currently no standardised format for the content of such alert cards across healthcare systems which represents an opportunity for oncology pharmacy practitioners to engage with other stakeholder organisations to ensure all these resources are accurate and reflect best practice to ensure patient safety.

Corticosteroids are agents which themselves require rigorous monitoring to reduce the risk of treatment-related adverse events including mood disturbances, diabetes insipidus, fractures and increased risks for opportunistic infections. Corticosteroids have been amongst the most commonly prescribed medications internationally given their widespread availability across healthcare systems, low treatment costs and well defined side effect profile.

Oncology pharmacists are therefore, well versed in managing patients receiving corticosteroids and are well positioned to utilise this experience to manage irAEs with published evidence. This illustrates the positive impact that effective management with this agent can have in successfully managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves. 25,36,44 Given the complexities of managing these multiple factors to consider all at the same time, maybe for the same patient, it is clear that pharmacist-led patient education interventions coupled with pharmacist management of irAEs are vital to managing irAEs while minimising the adverse effects of corticosteroids themselves.

Table 1. Summary of oncology pharmacist led interventions in managing irAEs.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Medications</th>
<th>Interventions</th>
</tr>
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<tbody>
<tr>
<td>General management</td>
<td>Corticosteroids (e.g. prednisone, dexamethasone)</td>
<td>Counsel patient on the adherence to corticosteroids; education patients on appropriate usage (dietary and time of administration); recommend long tapers when necessary.</td>
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<tr>
<td></td>
<td>Immunosuppressants (e.g. mycophenolate mofetil, infliximab)</td>
<td>Monitor toxicities in patients receiving immunosuppressants for management of irAE.</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis for infection</td>
<td>Assess the necessity for anti-infective prophylaxis and osteoporosis preventive therapies in patients receiving long term systemic corticosteroids or other immunosuppressants.</td>
</tr>
<tr>
<td></td>
<td>• Antibacterial</td>
<td></td>
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<tr>
<td></td>
<td>• Antifungal</td>
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<tr>
<td></td>
<td>• Antiviral</td>
<td></td>
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<tr>
<td></td>
<td>• Prophylaxis for osteoporosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Vitamin D and Calcium</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Thyroid hormone supplementation (e.g. levothyroxine)</td>
<td>Initiate thyroid hormone supplementation, and monitor thyroid stimulating hormones and free T4 as needed; monitor signs and symptoms of hypothyroidism.</td>
</tr>
<tr>
<td>Skin toxicities</td>
<td>Moderate to high potency topical steroids</td>
<td>Counsel patients on appropriate usage of topical products for skin toxicities.</td>
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<tr>
<td></td>
<td>Anthistamines (e.g. loratadine, cetirizine)</td>
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<tr>
<td></td>
<td>Emollient (e.g. urea cream)</td>
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<tr>
<td></td>
<td>if severe, consider systemic corticosteroids</td>
<td></td>
</tr>
<tr>
<td>Diarrhea/colitis</td>
<td>For mild symptoms: anti-diarrheal (such as loperamide)</td>
<td>Instruct patients on appropriate use of anti-diarrheal medication.</td>
</tr>
<tr>
<td></td>
<td>For severe symptoms: hold immune checkpoint inhibitors and consider high dose corticosteroids, and if no improvement, infliximab</td>
<td>Counsel on the importance of hydration and electrolyte replacement.</td>
</tr>
<tr>
<td></td>
<td>Electrolyte replacement therapies</td>
<td>Monitor fluid status and electrolytes as needed.</td>
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</tbody>
</table>

*Note: This is not an exhaustive list of potential adverse events associated with immune checkpoint inhibitors.
entry-to-practice level medical, nursing, pharmacy, pharmacy technician and assistant, and other allied health school curriculum in cancer care, post-graduate education in oncology care, and post-graduate fellowship training in oncology care. Oncology pharmacy practitioners are also an important contributor to continuing education of the MHT including participation in journal clubs, drug information requests and education through patient care discussions.

**Clinical governance**

Statement 3: Oncology pharmacy practitioners should be involved, within scope of practice, in clinical governance to support the efficient, safe, effective and optimal use of immunotherapy with immune checkpoint inhibitors.

Oncology pharmacy practitioners have a documented role to play in developing clinical governance processes which support the safe and effective use of medicines. Within the treatment of malignant disease, oncology pharmacy practitioners have been instrumental in introducing a range of now commonly accepted governance measures, including development of standardised chemotherapy treatment protocols, managing information systems and electronic documents and alerts, formal guidance supporting and informing evidence-based practice, and treatment algorithms which support management of side effects of chemotherapy treatments. National and international oncology pharmacy associations have made significant contributions to clinical governance through publication of literature which outlines and supports best practice and promotes the roles of the pharmacy team within the wider MDT.

The ISOPP Immunotherapy Task Force conducted a survey to explore the role of oncology pharmacy practitioners in the field of immunotherapy. One of the goals of the task force was to identify what contemporary governance support is available across responding healthcare systems in the field of immunotherapy and use this information to facilitate an ISOPP position statement. Core concepts to help standardise best practice principles can be used to help guide practice in local, regional and national levels.

A literature review was also completed to identify best practices. There are clear needs for development of protocols to outline best practices around oncology pharmacist-led irAE services. While oncology pharmacy practitioners have demonstrated significant positive impact on patient care in this area, the clinical responsibilities incurred go beyond those routinely expected of oncology pharmacists in contemporary practice. In order to support more oncology pharmacists to provide care for patients with irAEs, protocols which outline best practices around management of corticosteroids, including guidance around management of steroid tapering and management of irAEs which return following dose reduction, would help standardise best practice in this area.

Oncology pharmacists also play a key role in ensuring the dosing of the immune checkpoint inhibitor follows their institutional guidelines and policies. For example, options for dosing include weight-based dosing up to a maximum dose (i.e. pembrolizumab 2 mg/kg IV up to a maximum of 200 mg IV every 3 weeks), and flat dosing (i.e. pembrolizumab 200 mg IV every 3 weeks for all patients). In addition, it is important that oncology pharmacists are updated of any changes in immune checkpoint inhibitor dosing as the recommendations may change based on evolving evidence. For example, when avelumab was introduced onto the market, the dosing was 10 mg/kg IV every 2 weeks. This was updated in 2020 to a recommended flat dose of 800 mg IV every 2 weeks for all patients.

Some of the immune checkpoint inhibitors have more than one recommended dosing schedule (e.g. nivolumab can be given every 2 or 4 weeks and pembrolizumab can be given every 3 or 6 weeks). Oncology pharmacists play a role to ensure the dosing frequency for the immune checkpoint inhibitor is appropriate. In addition, they play a key role in advising on best practices for computer systems to support clinical care.

As indications for use continue to expand for some immune checkpoint inhibitors, it is important for oncology pharmacists to be able to ensure the correct dosing and frequency is used. For example, for advanced renal cell carcinoma, nivolumab may be dosed at 3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then nivolumab single agent 240 mg every 2 weeks or 480 mg every 4 weeks. However, the dosing and frequency are different when nivolumab is dosed at 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks for malignant pleural mesothelioma.

Oncology pharmacists play an important role to ensure regional or national best practices are followed by prescribers. Their role to ensure the correct regimen based on the patient’s clinical pathology and PD-L1 expression is important. For example, for patients with metastatic or unresectable head and neck squamous cell carcinoma, pembrolizumab monotherapy is only indicated for the first-line treatment in patients whose tumours express PD-L1 Combined Positive Score (CPS) equal to or greater than 1%. It is important that these clinical criteria regarding scoring be added to best practice standards to ensure oncology pharmacists have this information at their disposal when conducting a clinical review of the prescriber’s orders.

Oncology pharmacists provide guidance to the creation of appropriate sequencing and supportive care for physician order sets. With the introduction of the combination of immune checkpoint inhibitors with chemotherapy backbones, it is important that the appropriate supportive care be built into the treatment protocols. In addition, if there
are instances in which one drug should be given before another, the oncology pharmacist is positioned to provide that guidance to the MDT as the protocol is developed.

Oncology pharmacists, pharmacy technicians and assistants are important for assisting with financial management of immune checkpoint inhibitors. Oncology pharmacy practitioners may fill the role of drug access navigators and assist patients to navigate drug coverage through public coverage, third party insurance and manufacturer assistance programmes. In publicly funded institutions, oncology pharmacists provide guidance on cost containment of immune checkpoint inhibitors by adopting dose rounding policies that follow their institutional policies. For example, if a 54 kg patient receives a dose of 1 mg/kg (equals 54 mg), the dose rounding could be to the nearest vial for this patient (50 mg) if the institutional policies allow for 10% variance. An example of cost containment is adoption of institutional dose rounding policies and immune checkpoint inhibitor dose rounding or banding automatically embedded into computer physician order sets. Another example of cost containment that is used by oncology pharmacists is to have “immune checkpoint inhibitor” day(s) in their treatment centre. In this way, it is possible to minimise drug wastage.

Research and development

Statement 4: Oncology pharmacy practitioners should be involved in and support research and development in the field of immunotherapy.

Oncology pharmacy practitioners have an emerging role within research and development in the field of immunotherapy. This mirrors developments in research more generally in which oncology pharmacy practitioners are undertaking a more active role and moving beyond traditional responsibilities in facilitating clinical trials through management of investigational medical products. Indeed, the potential of utilising oncology pharmacists’ unique skill set as experts in medicines has been recognised by trial sponsors with increasing numbers of clinical trials employing oncology pharmacists as principle investigators.12,54

In addition, oncology pharmacy practitioners are closely involved in the evaluation of medication use and management of toxicities.12 These aspects of pharmacy practice are ideal for research and quality improvement studies of some unique features of checkpoint inhibitor immunotherapy. For example, the optimal dosing regimens of checkpoint inhibitors are still unclear,55,56 particularly within the context of minimising drug wastage.57,58 Similarly, the optimal management and application of consensus management guidelines of irAEs is still in the early phase of development.59 Indeed, the classification and grading of irAEs are an ongoing area of discussion which may benefit from oncology pharmacist research engagement (Table 2).59,60

Table 2. Potential research directions for immunotherapy with checkpoint inhibitors.

<table>
<thead>
<tr>
<th>Clinical trials on efficacy and outcomes</th>
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<tr>
<td>Optimizing dosing regimens</td>
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<tr>
<td>Patient reported outcomes</td>
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<tr>
<td>Classifying, grading and managing irAEs</td>
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<tr>
<td>Pharmacoeconomics analyses</td>
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<td>Drug utilisation reviews</td>
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Conclusion

Immunotherapy represents a new and effective therapy option in the treatment of malignant disease. In order to support the safe and effective use of these novel agents, pharmacy teams must develop a new set of skills to ensure patients are able to benefit from the clinical advantages these agents provide while minimising the risk of side effects. This position paper has identified four distinct areas where oncology pharmacy practitioners can provide particular benefit to patient care: clinical oversight, education and training, clinical governance, and research and development.

Oncology pharmacists have high potential to be involved in the treatment of patients receiving immunotherapy, from the prescription until long after treatment has finished, as well as in the constant development of these new therapies or combinations with traditional or already approved agents.

The ISOPP Immunotherapy Task Force recommends that health care systems around the world recognise and support the unique role of oncology pharmacy practitioners in being involved in the treatment and caring of patients receiving immunotherapy with checkpoint inhibitors.

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# Appendix 1: ISOPP Immunotherapy Task Force Members

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